CLAIMS

What is claimed is:

1. A method of treating a central nervous system metastatic cancer sensitive to the combination of radiation, supplemental oxygen, and efaproxiral sodium in a host having a central nervous system metastatic cancer comprising:

administering radiation to the host;

administering efaproxiral sodium to the host, and

administering supplemental oxygen to the host,

wherein the radiation, supplemental oxygen, and efaproxiral sodium are administered in amounts effective to cause an arrest or regression of the central nervous system cancer in the host.

2. The method of claim 1, comprising:

A) administering radiation to the host;

B) administering efaproxiral sodium to the host, wherein the efaproxiral sodium is administered at a dosage selected from the group consisting of

i) 100 mg/kg, if conditions are conditions selected from the group consisting of:

a) radiation treatment day 1, the host is a male $\leq$ 95 kg, and SpO_2 is $\geq$ 93%

b) radiation treatment day 1, the host is a female $\leq$ 70 kg, and SpO_2 is $\geq$ 93%

c) radiation treatment day 2-10, the dose was 75 mg/kg on the previous dosing day, and SpO_2 while breathing room air is currently $\geq$ 93% and no adverse event occurred on the previous dosing day, wherein said adverse event is selected from the group consisting of supplemental oxygen administration > 3 hours after end-infusion of efaproxiral sodium before SpO2 while breathing room air returned to $\geq$ 90% on the previous dosing day, the patient experienced nausea and/or vomiting (grade 2 or higher) or clinically significant hypotension associated with efaproxiral sodium within 12 hours after efaproxiral sodium administration on the previous dosing day, and the patient developed hypoxemia which required treatment after discharge on the previous dosing day;

d) radiation treatment day 2-10, SpO_2 is >90%, the dose was 100

mg/kg on the previous day and no adverse event occurred on the previous day, wherein said adverse event is selected from the group consisting of supplemental oxygen administration > 3 hours after end-infusion of efaproxiral sodium before SpO2 while breathing room air returned to ≥ 90% on the previous dosing day, the patient experienced nausea and/or vomiting (grade 2 or higher) or clinically significant hypotension associated with efaproxiral sodium within 12 hours after efaproxiral sodium administration on the previous dosing day, the patient developed hypoxemia which required treatment after discharge on the previous dosing day, and SpO_2 while breathing room air is 90-92% but was ≥ 93% on the previous dosing day;

ii) 75 mg/kg, if conditions are conditions selected from the group consisting of:

a) radiation treatment day 1, the host is a male > 95 kg, and SpO_2 is ≥ 93%,

b) radiation treatment day 1, the host is a female > 70 kg, and SpO_2 is ≥ 93%,

c) radiation treatment day 1 and SpO_2 is 90-92%,

d) radiation treatment day 2-10, the previous day's dose was held, SpO_2 is 90-92% and SpO_2 was 90-92% on the dosing day that led to holding the efaproxiral sodium dose,

e) radiation treatment day 2-10, the previous day's dose was held, and SpO_2 is ≥ 93%,

f) radiation treatment day 2-10, the previous day's dose was 100 mg/kg, and an adverse event occurs, wherein said adverse event is selected from the group consisting of supplemental oxygen administration > 3 hours after end-infusion of efaproxiral sodium before SpO2 while breathing room air returned to ≥ 90% on the previous dosing day, the patient experienced nausea and/or vomiting (grade 2 or higher) or clinically significant hypotension associated with efaproxiral sodium within 12 hours after efaproxiral sodium administration on the previous dosing day, the patient developed hypoxemia which required treatment after discharge on the previous dosing day, and SpO_2 while breathing room air is 90-92% but was ≥ 93% on the previous dosing day, and

g) radiation treatment day 2-10, SpO_2 is >90%, and the dose was 75 mg/kg on the previous day and no adverse event occurred on the previous day, wherein said adverse event is selected from the group consisting of supplemental oxygen administration >

3 hours after end-infusion of efaproxiral sodium before SpO2 while breathing room air returned to ≥ 90% on the previous dosing day, the patient experienced nausea and/or vomiting (grade 2 or higher) or clinically significant hypotension associated with efaproxiral sodium within 12 hours after efaproxiral sodium administration on the previous dosing day, the patient developed hypoxemia which required treatment after discharge on the previous dosing day, and SpO_2 while breathing room air is 90-92% but was ≥ 93% on the previous dosing day; and

iii) 0 mg/kg, if conditions are conditions selected from the group consisting of:

a) SpO_2 is < 90%,

b) radiation treatment day 2-10, the dose was 75 mg/kg on the previous day and an adverse event occurs, wherein said adverse event is selected from the group consisting of supplemental oxygen administration > 3 hours after end-infusion of efaproxiral sodium before SpO2 while breathing room air returned to ≥ 90% on the previous dosing day, the patient experienced nausea and/or vomiting (grade 2 or higher) or clinically significant hypotension associated with efaproxiral sodium within 12 hours after efaproxiral sodium administration on the previous dosing day, the patient developed hypoxemia which required treatment after discharge on the previous dosing day, and SpO_2 while breathing room air is 90-92% but was ≥ 93% on the previous dosing day ,

c) radiation treatment day 2-10, the dose was 0 mg/kg on the previous day, SpO_2 is 90-92% but had been ≥ 93% on the previous dosing day that led to holding efaproxiral sodium

d) radiation treatment day 2-10, SpO_2 is >90%, and the dose was 0 mg/kg on the previous day and an adverse event occurs, wherein said adverse event is selected from the group consisting of supplemental oxygen administration > 3 hours after end-infusion of efaproxiral sodium before SpO2 while breathing room air returned to ≥ 90% on the previous dosing day, the patient experienced nausea and/or vomiting (grade 2 or higher) or clinically significant hypotension associated with efaproxiral sodium within 12 hours after efaproxiral sodium administration on the previous dosing day, the patient developed hypoxemia which required treatment after discharge on the previous dosing day, and SpO_2 while breathing room air is 90-92% but was ≥ 93% on the previous dosing day; and

C) administering supplemental oxygen to the host,

wherein the radiation, supplemental oxygen, and efaproxiral sodium are administered in

amounts effective to cause an arrest or regression of the central nervous system cancer in the host.

3. The method of claim 1, comprising:

A) administering radiation to a host having breast cancer and a central nervous system metastatic cancer and ;

B) administering efaproxiral sodium to the host, wherein the efaproxiral sodium is administered at a dosage selected from the group consisting of

i) 75 mg/kg, if conditions are conditions selected from the group consisting of:

a) radiation treatment day 1, SpO_2 is $\geq 90\%$, and creatinine ≤ 2.0 mg/dL;

b) radiation treatment day 4-10, the previous day's dose was 100 mg/kg, and an adverse event occurred on the previous day, wherein said adverse event is selected from the group consisting of supplemental oxygen administration ≥ 4 hours after end-infusion of efaproxiral sodium before SpO_2 while breathing room air returned to $\geq 90\%$ on the previous dosing day, the patient experienced nausea and/or vomiting (grade 2 or higher) or clinically significant hypotension associated with efaproxiral sodium within 12 hours after efaproxiral sodium administration on the previous dosing day, and the patient SpO_2 while breathing room air is $90 - 92\%$ and has decreased from a baseline of $\geq 93\%$ on the previous dosing day; and

c) radiation treatment day 2-10, SpO_2 is >90%, and the dose was 75 mg/kg on the previous day and no adverse event occurred on the previous day, wherein said adverse event is selected from the group consisting of ssupplemental oxygen administration $\geq$ 4 hours after end-infusion of efaproxiral sodium before SpO2 while breathing room air returned to $\geq 90\%$ on the previous dosing day, the patient experienced nausea and/or vomiting (grade 2 or higher) or clinically significant hypotension associated with efaproxiral sodium within 12 hours after efaproxiral sodium administration on the previous dosing day, and the patient SpO_2 while breathing room air is $90 - 92\%$ and has decreased from a baseline of $\geq 93\%$ on the previous dosing day; and

ii) 100 mg/kg, if conditions are radiation treatment day 3-10, the dose was 75 mg/kg on the previous two dosing days or 100 mg/kg on the previous dosing day, and SpO_2 while breathing room air is $\geq 90\%$ and no adverse event occurred on the previous

dosing day, wherein said adverse event is selected from the group consisting of supplemental oxygen administration ≥ 4 hours after end-infusion of efaproxiral sodium before SpO2 while breathing room air returned to ≥ 90% on the previous dosing day, the patient experienced nausea and/or vomiting (grade 2 or higher) or clinically significant hypotension associated with efaproxiral sodium within 12 hours after efaproxiral sodium administration on the previous dosing day, and the patient SpO_2 while breathing room air is 90 – 92% and has decreased from a baseline of ≥ 93% on the previous dosing day; and

iii) 0 mg/kg, if conditions are conditions selected from the group consisting of:

a) SpO_2 is < 90%,

b)creatinine is > 2.0 mg/dL;

c) the patient developed hypoxemia which required treatment on the previous treatment day;

d) RT day 2-10, the dose was 75 mg/kg on the previous day and an adverse event occurred, wherein said adverse event is selected from the group consisting of supplemental oxygen administration > 3 hours after end-infusion of efaproxiral sodium before SpO2 while breathing room air returned to ≥ 90% on the previous dosing day, the patient experienced nausea and/or vomiting (grade 2 or higher) or clinically significant hypotension associated with efaproxiral sodium within 12 hours after efaproxiral sodium administration on the previous dosing day, the patient developed hypoxemia which required treatment after discharge on the previous dosing day, and SpO_2 while breathing room air is 90-92% but was ≥ 93% on the previous dosing day; and

C) administering supplemental oxygen to the host,

wherein the radiation, supplemental oxygen, and efaproxiral sodium are administered in amounts effective to cause an arrest or regression of the central nervous system cancer in the host.

4. The method of claim 1, wherein the radiation is administered in at least about 3 Gray (Gy) fractions at least once every day for ten days to a treatment volume.

5. The method of claim 1, wherein the radiation is administered in fractions, wherein 10 fractions are administered to an initial treatment volume.

6. The method of claim 1, wherein a total of at least about 30 Gy of radiation is administered to the host.

7. The method of claim 1, wherein radiation is administered to a whole brain of the host.

8. The method of claim 1, wherein the efaproxiral sodium is administered via a route selected from the group consisting of intravenously including via a central venous access device, or via a peripheral route, via continuous infusion, and intraarterially.

9. The method of claim 1, wherein the efaproxiral sodium is administered at an initial dosing level of at least about 75 mg/Kg/day.

10. The method of claim 1, wherein the efaproxiral sodium is administered so as to achieve a RBC conentration of greater than about 483 μg/ml.

11. The method of claim 1, wherein the metastatic cancer is derived from a primary cancer selected from the group consisting of lung, breast, melanoma, renal, and colorectal.